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Using genetic parameters to predict somatisation in females with heroin dependence

Kadir Uludag [1], Hang Su [1], Haifeng Jiang [1], Jiang Du [1], Na Zhong [1], Min Zhao [1,2,3]

1. *Shanghai Jiao Tong University, School of Medicine, Mental Health Center, China*
2. *Shanghai Key Laboratory of Psychotic Disorders, Shanghai, China*
3. *CAS Center for Excellence in Brain Science and Intelligence Technology (CEBSIT), Chinese Academy of Sciences, Shanghai, China*

Summary

Background. Heroin dependence is a severe psychiatric disorder that is often associated with various comorbidities, including somatic symptoms such as pain, anxiety, weakness, tremors, muscle pain, sleep disturbances, and shortness of breath, as well as personality disorders, mood, and psychotic disorders. While heroin use may initially alleviate these symptoms, it can also exacerbate them over time. There is a notable gap in our understanding of the genetic factors, such as catechol-O-methyltransferase (COMT), that can potentially aid in predicting susceptibility to somatisation. **Aim.** We aimed to utilise specific genetic parameters, such as COMT and stress-related factors, to indicate the somatisation status accurately. **Methods.** Only female patients with heroin dependence were recruited for the study (N=263). We have compared the groups with and without somatisation. Cross-validation was conducted to validate the results obtained from the machine learning (ML) process. **Results.** Random Forest (RF) demonstrated exceptional performance in predicting somatisation status, achieving an impressive accuracy of 99% (sensitivity:100%, specificity:98%). The mean accuracy of cross-validation for the model was 90%, indicating a reliable performance. **Conclusions.** The genetic factors investigated in this study did not show any association with the status of heroin use. We achieved a successful prediction of somatisation status solely based on genetic parameters.

Key Words: Heroin addiction; heroin dependence; heroin treatment; drug treatment; drug addiction; psychotic disorder; somatisation symptoms

1. Introduction

Heroin is a highly addictive substance [18] and has a significant impact on individuals around the globe [16, 51, 87]. The rate of heroin use in teenagers is a concern [27]. It is associated with negative mood [72], poor oral health [1], accelerated ageing [12] and somatic symptoms such as sleep problems [56], depression [19, 73], anxiety [15] and other bodily issues. Moreover, the process of somatisation has the potential to intensify pre-existing psychiatric symptoms. Furthermore, studies found structural changes in heroin-dependent individuals [101]. Somatic disorders involve physical symptoms that cannot be explained medically [40, 60, 66, 91].

Patients with somatic disorders exhibit a wide range of heterogeneity [59, 91]. The existing literature does not provide a definitive understanding of the association between substance use and somatisation symptoms [2]. Furthermore, there is a frequent tendency to misinterpret somatisation symptoms as withdrawal symptoms due to the overlapping nature of these two types of symptoms [33]. Somatisation is a phenomenon that may often be overlooked or dis-

Corresponding author: Min Zhao, Shanghai Jiao Tong University; 600 Wangpin Nan Lu Street, 200030, China
Phone: 021-64387250; E-mail: drminzhao@smhc.org.cn

regarded within the field of general psychiatry [13]. Hence, it is crucial to explore the presence of somatisation symptoms and associated factors, such as genetics, through a thorough investigation of the [48], biological, sociodemographic characteristics, and personality disorders in patients with heroin dependence. In addition, machine learning (ML) methods enable the prediction of various scenarios by leveraging its computational capabilities.

2. Methods

Collectively, our study aimed to explore the complex relationship between heroin dependence and the presence of somatisation symptoms by comparing individuals with and without such symptoms. Furthermore, we endeavoured to forecast somatisation status using genetic parameters.

The study protocol obtained ethical approval from the institutional review board of the Shanghai Mental Health Center, School of Medicine, affiliated with Shanghai Jiao Tong University, adhering to the principles stated in the Declaration of Helsinki. Before participating, all patients confirmed their understanding of the informed consent and provided their signed consent forms. Interviews were conducted and recorded to ensure accurate documentation and facilitate future analysis. To maintain participant confidentiality, all interviews were recorded and subsequently anonymised. The genotyping of stress-related genes was performed using the TaqMan SNP genotyping assay, a widely utilised and reliable method in genetic analysis. Cross-validation techniques validated the machine learning outcomes associated with Random Forest (RF) and Neural Networks (NN) methodologies.

2.1. Participants

To be eligible for the study, patients had to meet the criteria for heroin dependence as outlined in the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), be at least 18 years old, and have a recent history of heroin use within the 30 days before compulsory rehabilitation.

A standard face-to-face interview was conducted with each participant within the first month of their rehabilitation program. These interviews were performed in a calm and comfortable room to ensure the participants' relaxed state. During the interviews, participants self-reported information related to their initial heroin use, including details such as their age at the time, the method of administration, the subjective response to the initial use, and the reasons behind their initial heroin use.

All patients in the study underwent a standardised compulsory rehabilitation program encompassing various essential elements for their recovery. This comprehensive program included daily exercise, manual labour, and regular education on relapse prevention. These interventions were implemented within the drug rehabilitation institutions, with the primary objective of facilitating the successful reintegration of the patients into their respective communities upon completion of the program.

For the present study, only female participants were selected. Among female participants, the average first-drug-use age was "21.79". Most of the participants had no family members living with them. Most of the participants were not employed. The missing data was less than 6 per cent.

Individuals who have a history of severe medical conditions that may impact the study outcomes, such as neurological disorders or traumatic brain injury, were excluded. Patients who could not comply with study requirements, such as attending regular appointments or completing study assessments, were also excluded.

2.2. Assessment

2.2.1. Demographic parameters and heroin use history

We collected demographic information, which included age, gender, education status (categorised as completed secondary school or not), marriage status (categorised as married or not married), and employment status (categorised as employed or unemployed). Additionally, the dose of heroin consumed within the previous month was measured and recorded as a quantitative variable.

2.2.2. Genetic parameters

In this study, the following genetic parameters were used: rs1544325, rs174696, rs174699, rs4680, rs4818, rs737866, rs933271, rs12953076, rs4458044, rs242924, rs17689966, rs1715751, rs3792738, rs32897, rs10062367, rs1875999.

Some of the genetic parameters were related to Catechol-o-methyltransferase (COMT) gene (e.g., rs1544325, rs174696, rs4680, rs4818, rs737866, rs933271) while some of the parameters were related to stress (e.g., rs1715751, rs3792738, rs32897, rs10062367, and rs1875999).

2.2.3. Symptom Checklist 90

Regular revisions are required for the Symptom Checklist (SCL-90), which serves as a screening scale [14]. It showcases a distinctive compilation of concise and multidimensional psychological assessment instruments tailored specifically for evaluating psychological symptoms [17]. Regular revisions of the SCL-90 are essential to incorporate advancements in research and clinical understanding, ensuring its

relevance and reliability in the ever-evolving field of psychological assessment.

2.2.4. The Barratt Impulsiveness Scale

The Barratt Impulsiveness Scale (BIS) is a commonly used questionnaire that evaluates impulsivity. Over time, the BIS has gained significant popularity and is now regarded as one of the most extensively employed measures of impulsivity in research. Higher scores on the BIS indicate more substantial levels of impulsivity. Within the BIS framework, the BIS-11 is explicitly a psychological assessment tool that evaluates impulsivity across three sub-traits: attentional impulsiveness, motor impulsiveness, and non-planning impulsiveness **[94]**.

2.2.5. Scales for the personality assessment

In this study, we employed a range of scales to assess various personality disorders, including depressive, paranoid, schizotypal, schizoid, histrionic, narcissistic, borderline, and antisocial personality disorders.

2.2.6. Medical Outcomes Study Social Support Scale

The Medical Outcomes Study Social Support Scale (MOS) is a reliable tool developed by **[47]**.

MOS allows researchers to measure participants' subjective experience, which can be used to understand the underlying psychological processes.

2.2.7. Zuckerman–Kuhlman Personality Questionnaire

Trait theory raises a significant inquiry regarding the number of essential traits required to describe personality and the specific nature of these traits comprehensively. The Zuckerman-Kuhlman Personality Questionnaire (ZKPQ) is designed to assess a five-factor model, contributing to exploring this question **[29]**.

2.3. Machine Learning Models

2.3.1. Random Forest

Random Forest (RF) is a machine learning (ML) technique used in various studies, including psychology **[5]**, bioinformatics **[79]**, psychiatry **[98]**, and computer sciences **[22]**. Leo Breiman's RF algorithm has established itself as a widely adopted and essential tool for data analysis **[10]**. This algorithm, introduced by Breiman, has gained significant popularity due to its effectiveness and versatility across various domains.

2.3.2. Random forest settings used in this study

Considering various settings, including the test size, is essential when utilising RF. Number of trees was set to "100 ". Also, the test size was set to "0.3". Sci-kit Learn package was used to conduct ML analysis **[77]**. These settings were chosen to ensure a robust and reliable data analysis within the RF framework.

2.4. Statistical Analysis

Demographic data encompassed variables such as age, gender, education (categorised as completed secondary school or not), marriage status (categorised as married or not married), and employment status (categorised as employed or unemployed). Participants who reported experiencing somatisation symptoms were coded as "1," while those without such symptoms were coded as "0."

The chi-square test was employed to examine the association between two categorical variables. Missing categorical variables were replaced with the mode value while missing non-categorical variables were replaced with the mean value. Correlation tests, either Spearman or Pearson, were utilised based on the normality of the parameters. The p-value threshold was set at 0.05.

Similarly, participants who reported having hallucinations were coded as "1," while those without hallucinations were coded as "0." Subsequently, the two groups were compared in terms of various factors. The Mann-Whitney U test or Independent Samples t-test was used depending on the normality of the parameters.

In this study, aside from assessing various parameters, the relapse status of all participants was meticulously tracked and coded as a binary categorical variable. The alleles were represented as categorical variables by assigning unique codes or labels to each allele category.

3. Results

3.1. Clinical characteristics results

There was no observed association between somatisation status and the following parameters: relapse status, employment status, marriage status, and heroin dose ($p>0.05$, **Table 1**).

According to the Mann-Whitney U test, we found a significant relationship between somatisation and the following variables: disorderly conduct behaviour, vagrancy, drunk driving car, SCL 60, SCL 79, SCL 78, and SCL 90.

There were no noteworthy correlations found between somatic disease and the genetic parameters rs12953076, rs4458044, rs242924, rs17689966,

rs3792738, rs32897, rs10062367, and rs1875999 (all with p-values greater than 0.05).

Furthermore, no association was found between somatic disease and the following parameters: hallucinogen use, marriage status, employment, and alcohol use (all with p>0.05).

3.2. *Machine Learning results*

The RF model demonstrated exceptional performance with an accuracy of 99% (sensitivity: 100% and specificity: 98%). The top five predictive parameters identified were rs4458044, rs1875999, rs3792738, rs1715751, and rs174699.

On the other hand, the NN model achieved an accuracy of 82% (sensitivity: 5% and specificity: 94%). The most influential parameters in the NN model were rs3792738b, rs174699, rs1544325, rs1875999b, and rs933271.

Cross-validation results further supported the RF model's reliability, with an accuracy of 90%. The NN model also demonstrated consistent performance with a cross-validation accuracy of 83% (**Table 2**).

4. Discussion

Based on the key findings, no significant associations were found between the genetic parameters (rs174696, rs174699, rs4680, rs4818, rs737866, rs933271, rs12953076, and rs44458044) and somatisation status (all, p>0.05).

Additionally, utilising the Random Forest (RF) model, we achieved a remarkable accuracy of 99% in successfully predicting somatisation status, with a sensitivity of 100% and specificity of 98%. Meanwhile, the Neural Networks (NN) model yielded an accuracy of 82%, with a sensitivity of 5% and specificity of 94%, for predicting somatisation status. Cross-validation results further supported the RF model's reliability, with an accuracy of 90%. The NN model also demonstrated consistent performance with a cross-validation accuracy of 83%.

The finding that these specific genetic parameters are not associated with somatisation status provides valuable information for researchers working to understand better and treat somatic symptom disorders. However, further research is needed to understand the complex interplay between genetics, environment, and psychological factors that contribute to the development of these disorders. Also, a previous study mentioned cultural aspects of the somatisation **[30]**. They are potential confounding factors in our study. Regrettably, our study did not incorporate the essential cultural parameters specific to our Chinese participants. Furthermore, our analysis revealed no significant association between somatisation status and subscale scores of the Medical Outcomes Study Social Support Scale (MOS) (p-value less than 0.05).

To understand our study findings regarding somatisation, we should understand the classification of somatisation and confounding factors. Furthermore, publication-related bias can influence the presence of confounding factors in the literature, as researchers tend to avoid reporting negative results.

Table 1. Statistics of comparison tests

Variables	T, Z, or chi-square value	P- Value
Employment Status	3.091	p>0.05
Marriage Status	3.643	p>0.05
Dose of Heroin	-0.468	p>0.05
Relapse Status	1.206	p>0.05
MOS total scale score	-0.730	p>0.05
BIS 10	-2.148	p<0.05
BIS 11	-2.100	p<0.05
BIS total scale score	-2.338	p<0.05
Personality Disorders		
Avoidant	-0.139	p>0.05
Dependent	-1.408	p>0.05
Obsessive compulsive Disorder	-0.757	p>0.05
Antisocial personality disorder	-0.433	p>0.05
Negativistic Personality Disorder	-0.757	p>0.05
Other Substances		
Hallucinogen Use	0.081	p>0.05
Tranquilizer Use	0.044	p>0.05
Inhalation Use	0.437	p>0.05
Alcohol Use	1.959	p>0.05
Amphetamine Use	0.899	p>0.05
Cocaine Use	0.568	p>0.05
Genetic Factors		
rs174696	3.441	p>0.05
rs174699	3.573	p>0.05
rs4680	1.797	p>0.05
rs4818	3.401	p>0.05
rs737866	2.178	p>0.05
rs933271	3.104	p>0.05
rs12953076	-0.952	p>0.05
rs44458044	-0.012	p>0.05
rs32897	5.998	p>0.05
rs1544325	-0.314	p>0.05

BIS, Barratt Impulsiveness Scale; MOS, Medical Outcomes Study Social Support Scale

Table 2. Machine learning score according to Random Forest

	Random Forest	Neural Networks
Accuracy	99%	82%
Precision	86%	50%
Recall	99%	50%
Sensitivity	100%	5%
Specificity	98%	94%

4.1. Classification of somatisation

A comprehensive and universally accepted classification system for somatisation symptoms is crucial for several reasons. Firstly, it allows for a standardised approach to assessing and diagnosing somatisation disorders, ensuring consistency across healthcare professionals and settings. A precise classification system enables clinicians to identify and differentiate between somatic symptoms and disorders, facilitating accurate diagnosis and appropriate treatment planning. Furthermore, it is worth noting that different types of somatisation may exhibit correlations with specific somatisation symptoms. Somatisation and heroin dependence are two distinct conditions that can have significant impacts on an individual's physical and mental well-being. Understanding the classification of these conditions helps in their diagnosis, treatment, and management.

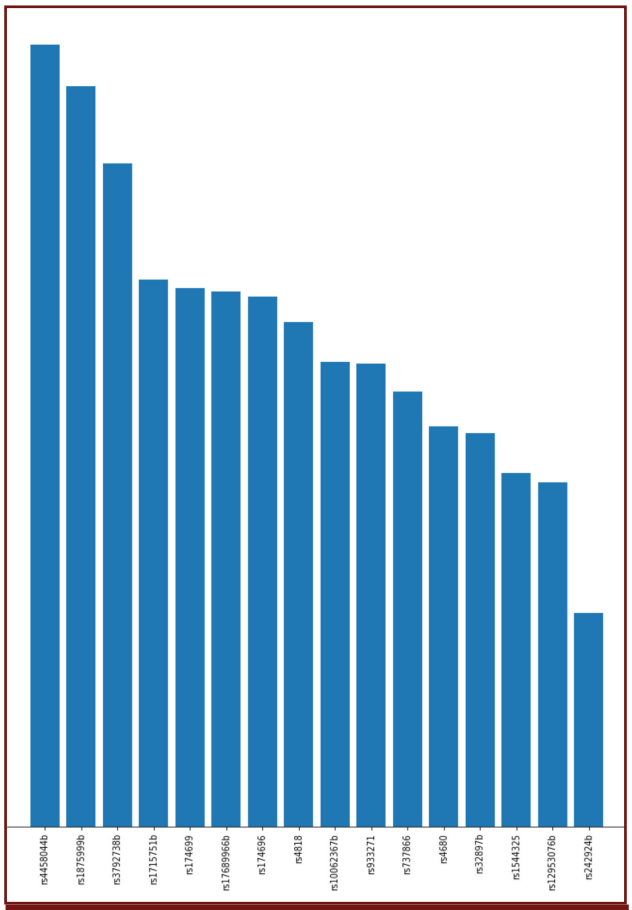

Figure 1. Most Predictive Factors, according to Random Forest

Moreover, it is of utmost importance to establish a universally recognised classification system to manage patients presenting with functional somatic symptoms effectively [24]. Several definitions of somatisation deal with the fundamental problem that many patients present with physical symptoms for which a conventional pathology cannot be detected [83]. The severity of somatisation symptoms is related to various factors such as psychological [8], biological [49], genetics [48], epigenetics [75], and environmental [42].

The literature on somatisation status and genetics is exceptionally scarce. A previous study investigated the association between somatisation and panic disorder. The implementation of the diagnostic criteria for somatisation disorder as specified in the DSM-IV led to a reduction in the occurrence of comorbidity with panic disorder. The study indicates that somatisation should not be considered a subtype or variation of panic disorder, as these disorders can coexist independently without sharing a genetic predisposition [7].

The severity of somatisation was discovered to have a significant association with the neural response [53], and somatic withdrawal exhibited a connection with the expression of c-Fos [3]. Furthermore, somatisation features could be significant when formulating classification criteria [81]. A previous proposition entails a shift in perspective, wherein unexplained symptoms are recontextualised as manifestations of a functional disruption in the nervous system and advocate for integrating treatments classified as "psychiatric" into the general medical care [89]. Recognising that not all unexplained symptoms can be categorised as somatic or psychiatric symptoms is essential. By acknowledging the complexity and intricacies of unexplained symptoms, healthcare professionals can strive for a more holistic and patient-centred approach. This may involve conducting thorough medical evaluations, considering a range of potential factors, and collaborating across disciplines to explore all possible explanations. The classification of somatisation provides a framework for categorising the complex manifestation of physical symptoms, leading to improved diagnosis and overall patient care. Establishing clear and objective criteria for defining and treating somatisation symptoms is crucial.

4.2. Heroin use, somatisation and psychological symptom severity

Heroin use is associated with specific psychological symptoms such as mood disorders, attention deficit hyperactivity [58], anxiety and depression [62]. Heroin is used as a means to alleviate specific psychiatric symptoms. Moreover, individuals may also utilise these substances to seek out new and unique experiences.

There are several psychological factors associated with addiction. For instance, anxiety plays a crucial role in addiction [63]. Research suggests a notable association between increased substance use and elevated levels of depression among individuals [74]. Improved access to heroin leads to increases in heroin use and somatic signs [97]. Patients with heroin dependence show perceptual disturbances [50].

Interestingly, heroin injection was negatively associated with psychosis [52]. Also, other studies found a negative relationship between the severity of positive symptoms and heroin use. However, it is crucial to consider confounding factors, such as heroin dose and route of administration, when examining the relationship between gender, heroin use, and genetics. These factors can significantly influence the effects of heroin and contribute to differences observed between males and females; the high severity of heroin addiction was also related to psychotic experiences [82]. The number of somatic complaints has been found to correlate with depression [15]. The attachment may influence the substance preferences [85] and may be related to the severity of somatisation-related psychological symptoms (e.g., anxiety and depression).

Additionally, physical abuse was associated with increased use of heroin [23]. Physical abuse can have far-reaching consequences, extending beyond the immediate harm inflicted. In addition to its evident physical effects, such abuse can also give rise to a range of psychological symptoms.

The heroin-dependent patients exhibited a prevalence of risky sexual behaviours [32]. Heroin use has been associated with an increased risk of engaging in unsafe sexual practices, which can have detrimental consequences, including the development of inflammatory issues and the transmission of sexually transmitted diseases (STDs). The link between heroin use and inflammatory changes is particularly relevant when considering the potential impact on STDs. The use of heroin can negatively impact an individual's ability to make sound judgments and decisions, resulting in a higher likelihood of engaging in risky sexual behaviours. These behaviours may include unprotected sex or having multiple sexual partners, thereby increasing the risk of contracting STDs.

Additionally, the use of heroin can have immunosuppressive effects. It is essential to recognise that the consequences of risky sexual behaviour and inflammatory changes extend beyond physical health. Psychological changes can also occur as a result of these interconnected factors.

The occurrence of mood disorders tends to be more prevalent among individuals with heroin dependence [20]. A research investigation analysed the relationships among heroin usage, emotion, and psychological disorders, along with their order, within the framework of co-occurring conditions. Those whose heroin dependence developed a year before their diagnoses indicated a higher occurrence of somatic comorbidity [61]. Also, emotional factors during childhood may be related to drug use behaviour. An instance of this can be seen in a study which demonstrated a correlation between emotional neglect and an escalation in dependence, specifically among females [88]. Additionally, heroin dose may be one of the essential factors as overdose status was associated with previous mental illness [11].

Deficits in decision-making shared by heroin represent vulnerabilities to addiction [100]. Methamphetamine (METH) has the potential to induce more severe psychiatric disorders compared to heroin. This is attributed to the impact of METH on the resting-state function of brain regions associated with mood regulation, auditory processing, and memory. These effects can contribute to the manifestation of psychotic symptoms associated with METH use [57]. However, the recent literature on brain imaging and the impacts of heroin is limited. Further studies should investigate the association between the side effects of heroin and somatic symptom severity.

Additionally, training emotion strategies may prevent craving [28]. Moreover, cognitive and behavioural therapies have demonstrated effectiveness in assisting individuals grappling with heroin dependence. These therapeutic approaches offer valuable tools and strategies to address the complex challenges associated with heroin addiction and support the process of recovery. Additionally, certain genetic factors may make some individuals more susceptible to the rewarding effects of heroin, increasing their likelihood of developing dependence.

The practical application of insights gained from brain imaging studies on heroin use or dependence can be multifaceted. Further studies employing brain imaging methods can provide valuable insights into the neurological consequences of heroin use or dependence. Knowing more about symptoms and severity of somatisation symptoms can help treat some psychiatric issues.

4.3. Somatisation symptoms and genetics

Genetics plays a role in various aspects of human health and behaviour, and it is believed to contribute

to the susceptibility of developing somatisation symptoms. Research suggests that certain genetic factors may influence an individual's vulnerability to somatic symptom disorders. In the present study, we have used COMT and stress-related genetic parameters.

Specific genetic factors could play a role in determining whether symptoms primarily manifest as physical sensations [93]. Another study discovers a link between polymorphisms in HTR2A, SERPINA6, and TPH2 genes and somatic symptoms [37]. In an alternative study, it was found that the HTR3C c.489C>A genetic variant is implicated in the development of depressive symptoms [9]. The presence of somatic symptoms and depression is prevalent in individuals with mitochondrial disease [25]. Hence, gaining a comprehensive understanding of the comorbidity between depression and somatisation is crucial.

Another study proposes that variations in the sensitivity of the dental pulp in older individuals may be influenced by the COMT gene, particularly about sex and temporomandibular disorder [68]. In conclusion, genetics plays a significant role in human health and behaviour, including somatisation symptoms. It has become increasingly clear through extensive research and studies that genetic factors contribute significantly to developing and expressing somatisation symptoms, encompassing physical complaints with no apparent medical explanation.

4.3.1. Gender differences and heroin use

Our study's sample exclusively comprised female participants, eliminating gender as a significant confounding factor. However, it is essential to acknowledge that the existing literature encompasses numerous studies that specifically examine gender differences in heroin use.

Heroin use among women is rising at a higher rate compared to men [65]. Gender differences have been observed, indicating that a higher proportion of women receive services for substance use. Moreover, after controlling for individual, service, and treatment organisational factors, it has been found that women demonstrate more significant reductions in substance use compared to men [64]. A common factor observed across various substance use disorders was the predominance of males [43]. Females are more vulnerable to the adverse consequences of abuse [26].

In the group of adult patients referred for ADHD treatment, men exhibited a higher prevalence of criminality, while women showed a higher prevalence of somatisation disorders [80]. In individuals diagnosed with psychotic disorders, being male was found to be correlated with an increased probability of engaging in drug abuse [71].

In a sample of patients seeking treatment for substance abuse, women with opioid, cannabis, and alcohol dependencies demonstrated a faster progression to entering treatment compared to men. These effects remained significant even after considering age as a factor. Interestingly, the age at which regular use of heroin and alcohol began did not differ between genders [35]. Additionally, men with first-episode psychosis were more likely than women to have used heroin [6]. Further, gender differences play a significant role in heroin use and its genetic underpinnings.

These results emphasise the significance of taking gender into account when researching substance use and when implementing treatment approaches. Further research is needed to understand these gender differences and develop tailored interventions to address them. Furthermore, researchers and practitioners need to recognise and examine the influence of culture on gender dynamics.

4.3.2. Somatisation and impulsivity symptoms

Impulsivity symptoms involve a tendency to act on urges without considering the potential consequences. This can manifest as impulsive behaviours like reckless spending, substance abuse, or engaging in risky activities. Furthermore, there is a recognised association between mood disorders and an increased likelihood of relapse in substance use [55].

The current study used the Barrat Impulsiveness Scale (BIS) to measure impulsivity symptoms. There is a likelihood that somatisation is related to impulsivity symptoms. Individuals who want to counteract the side effects of it may use heroin. The 10th and 11th subscale scores significantly differed between somatisation groups (I save regularly and squirm at plays or lectures).

A previous study claimed that heroin addiction may harm impulse control [76]. However, the literature on the relationship between the severity of somatisation symptoms and the presence of somatisation and impulsivity is scarce. Additionally, both somatisation and impulsivity can have a genetic basis, with certain genetic factors influencing the likelihood of experiencing these symptoms.

In conclusion, recognising and addressing somatisation and impulsivity symptoms can be crucial for promoting overall mental health and well-being, especially in heroin-dependent individuals.

4.4. Exploring the relationship between somatisation symptoms and compliance with rules and regulations

The existing literature needs to include comprehensive research on the association between the severity of somatisation symptoms and adherence to rules or regulations. Previous literature has mentioned the relationship between following rules and regulation and ADHD symptoms. Furthermore, attention was cited as one of the factors related to rules and regula-

tions. Similarly, several psychological theories have been proposed to explain the relationship between crime and psychological symptoms.

The presence of attentional processing difficulties in somatisation disorder indicates the existence of a disturbance at the neurophysiological level [39]. The presence of somatisation symptoms poses a risk for alcohol use [96]. Individuals who drink alcohol may suppress somatisation symptoms, while alcohol use may lead to criminal consequences such as traffic accidents. Also, heroin use is related to ADHD symptoms [58].

We found that driving under the influence of alcohol and disorderly conduct were seen to be associated with somatisation symptoms. Individuals may drink alcohol to suppress the severity of symptoms. Further research is necessary to fully understand the complex interplay between somatisation symptoms and criminal behaviour.

4.5. Confounding factors related to heroin dependence and somatisation symptoms

Confounding factors play a significant role in the relationship between heroin abuse and somatisation symptoms. Several intertwined factors can confound the interpretation and understanding of this association. It may lead to differences in the literature. Heroin abuse is a complex that can be influenced by a variety of confounding factors such as sociodemographic factors [90], gender [46], genetics [38], and accompanying mental health disorders such as depression and anxiety, and other factors such as routes of drug administration [99]. Applying the diagnosis of post-traumatic stress disorder (PTSD) may have clinical utility for patients with somatisation disorder, as it can identify a distinct subset of patients with somatisation who also display psychosocial impairment related to trauma exposure [92]. Thus, screening somatisation disorder patients for PTSD could reveal a subgroup and is one of the potential confounding factors in somatisation studies.

In a group of individuals seeking detoxification for opioid addiction and who engage in the use of multiple substances, racial distinctions may be significant factors to consider when developing treatment plans [44]. Therefore, race can be regarded as a potential confounding variable in this context. A consistent body of research indicates that women who have been victims of childhood sexual abuse face a substantially elevated risk of developing psychiatric disorders [45]. Additionally, engaging in physical activity has been shown to alleviate symptoms in functional somatic syndromes [34].

In a particular study, the regression analysis demonstrated a positive correlation between drug use and factors such as increasing age, academic underachievement, and parents being divorced [4]. Therefore, family factors (e.g., family relationships and childhood trauma) can play a significant role in addiction studies. A consistent body of research has consistently demonstrated that individuals who have a family history of addiction face an elevated risk of developing addictive behaviours themselves. In comparison to students without a family history of alcohol problems, students with positive family histories do not consume alcohol in higher quantities. However, they may be more susceptible to experiencing challenges related to alcohol and drug use [21]. Further research is needed to confirm the abovementioned associations between somatisation and relevant factors to broader populations (e.g., methamphetamine addiction and healthy participants). Therefore, a comprehensive understanding of these confounding factors is crucial to disentangle the complex interplay between heroin abuse and the severity of somatisation symptoms.

4.6. Polydrug use and somatisation symptoms

Polydrug abuse involves the concurrent use of multiple drugs, whereas somatisation symptoms encompass the manifestation of psychological distress through physical symptoms like headaches, tremors, heart palpitations, and abdominal pain. Thus, polydrug abuse is one of the major confounding factors in our study. Given that a significant portion of individuals who use heroin also consume other substances, such as alcohol, the presence of confounding factors becomes inevitable in human studies.

A study found that rates of smoking are around 23% but higher in patients with substance use disorder [41]. This trend reveals a significant correlation between substance abuse and tobacco addiction, necessitating targeted interventions and support for individuals dealing with both challenges simultaneously.

As heroin prices rose, heroin purchases decreased while reductions in purchases were less than price increases [78]. Thus, heroin price and polydrug use are the essential confounding factors that may affect treatment output and heroin use. In this study, we did not find a relationship between inhalation use and hallucinogen use in somatisation symptom groups ($p>0.05$). However, it is essential to acknowledge polydrug use as one of the critical confounding factors. By recognising the impact of heroin use, we can better understand the complexities involved in studying and addressing somatisation symptoms and their related factors.

4.7. Personality disorders and somatisation

The relationship between personality disorders and somatisation has been the subject of considerable research and clinical interest. Some personality

disorders can contribute to heightened anxiety levels, potentially increasing the vulnerability to heroin use. Those personality features may be related to risk-taking behaviour and can exacerbate the severity of somatisation symptoms.

The differentiation between histrionic personality disorder and somatisation disorder in clinical terms is not well-defined [70]. Individuals diagnosed with substance dependence exhibited a higher number of psychiatric symptoms throughout their lifetime when compared to individuals without substance dependence or cluster B personality disorder [54].

In a previous study, DBT had an indirect effect on somatisation through less emotional avoidance and suggested that the comorbid somatisation should be evaluated among those with borderline personality disorder in the context of the emotional avoidance [86]. The patients with multiple personalities exhibited a higher frequency of somatic symptoms than the remaining individuals [84]. In this study, we have used certain personality disorders as a parameter (obsessive-compulsive, avoidant, dependent, and antisocial). However, we did not find a significant relationship between those parameters and somatisation status. Further research may be necessary to investigate other potentially relevant factors contributing to the severity or presence of somatisation symptoms.

4.8. Treatment of heroin dependence and somatisation symptoms

The treatment of heroin dependence in individuals experiencing somatisation requires a comprehensive approach that addresses both the substance use disorder and the somatic symptoms. The literature is scarce on treating both heroin dependence and somatisation symptoms. People who have both a drug disorder and anxiety are more likely to report an unfulfilled need for treatment [67]. Consequently, it is crucial to recognise the associated psychological symptoms, such as depression and anxiety, to provide appropriate support and intervention.

In a study, the outcomes of interventions aimed at reducing heroin dependency were compared, specifically pharmacotherapy maintenance and incarceration. Evaluating the relative effectiveness of these interventions based on their consequences is a crucial aspect of the policy decision-making process. The quantitative data presented in the study can offer valuable insights relevant to evidence-based policy making [69]. The utilisation of heroin as a prescribed remedy should only be contemplated as a last resort once all alternative options have been thoroughly explored and exhausted [31].

Most somatisation symptoms are temporary and can be effectively addressed by modifying physician practices and appropriately implementing specific psychiatric and psychological treatments [95].

In conclusion, the treatment of heroin dependence and somatisation requires a comprehensive and multidimensional approach to address the complex interplay between physical and psychological factors. Both conditions pose significant challenges for individuals and healthcare providers, demanding a holistic and patient-centred approach.

Limitations. The current study is subject to several methodological limitations that should be acknowledged. Firstly, due to its cross-sectional design, we cannot establish a definitive temporal relationship between the independent variables and the onset or progression of heroin dependence. Additionally, our research did not utilise comprehensive scales specifically focused on somatisation. As a result, our findings may be influenced by the inclusion of individuals already experiencing mental health conditions, potentially reflecting the presence of psychiatric comorbidities such as anxiety and depression. Moreover, a significant portion of our psychological data, including somatisation symptoms and personality questionnaires, relied on self-report measures, which introduces the possibility of biased self-presentation.

Furthermore, it is essential to note that many of the patients with drug dependence were also using multiple substances, and only heroin urine tests were conducted during the follow-up period. This could potentially lead to an underestimation of the relapse rate in our study. Another limitation is the consideration of heroin dosage, as we only included information on the dosage from the previous month. In contrast, variations in dosage over time could act as confounding factors.

Moreover, the definition of somatisation utilised in our study may need more clarity and additional clarification or elaboration.

Overall, these methodological limitations, including the definition of somatisation and the heterogeneity of the studies, need to be considered when interpreting the findings. Future research should address these limitations to enhance the validity and generalizability of the results about somatisation status.

Suggestions for further studies. Conducting prospective studies will help to understand further the relationship between heroin use and the severity or presence of somatisation symptoms. Psychotic experiences can heighten the susceptibility to substance use [36]. Therefore, psychiatric problems underlying substance abuse should be targeted. Education campaigns can promote understanding, empathy, and early intervention for those experiencing somatisation symptoms. Automatic health systems can recognise people with somatic disorders based on their hospital visits since there must be apparent patterns to distin-

guish them. Also, genetic factors can be used to support automatised health systems.

5. Conclusion

In conclusion, it is essential to pay attention to somatisation symptoms in individuals with heroin dependence. Effective screening, diagnosis, and management of somatisation symptoms should be an integral part of the treatment plan for individuals with heroin dependence. Moreover, specific genetic parameters, such as the COMT gene, can potentially be utilised to predict the occurrence of somatisation.

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Contributors

The manuscript was authored by K.U. The final manuscript was reviewed and edited by H.S., M.Z., H.J., J.D., and N.Z. Data collection was carried out by H.S. and J.D. Statistical analysis was conducted by K.U.

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Conflict of interest

The Author declared no conflict of interest.

Ethics

The Author confirms that the submitted study was conducted according to the WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects. The study obtained ethical approval from the institutional review board of the Shanghai Mental Health Center, School of Medicine, affiliated with Shanghai Jiao Tong University All patients gave their informed consent to the anonymous use of their clinical data for this independent study.

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